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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
|-----------------|-------------|----------------------|---------------------|------------------|

10/032,592

10/24/2001

Firdous Farooqui

2065-181

8167

22471

7590

11/17/2004

EXAMINER

CEPERLEY, MARY

PATENT LEGAL DEPARTMENT/A-42-C  
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ART UNIT

PAPER NUMBER

1641

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                          |                     |  |
|------------------------------|--------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b>   | <b>Applicant(s)</b> |  |
|                              | 10/032,592               | FIRDOUS ET AL       |  |
|                              | <b>Examiner</b>          | <b>Art Unit</b>     |  |
|                              | Mary (Molly) E. Ceperley | 1641                |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 October 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-74 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-74 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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**1)** The final rejection of August 23, 2004 is hereby withdrawn in favor of the rejection set forth below.

**2)** The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**3)** Claims 1-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reddy et al (US 5,648,213) taken in combination with Garman et al (US 5,441,867).

Reddy et al describe a method of producing an oligonucleotide-protein conjugate which includes the steps of **a)** reacting an oligonucleotide containing an amine group with a heterobifunctional reagent having a first reactive group (e.g. N-hydroxysuccinimide) specific for the amino groups of the oligonucleotide and a second reactive group (e.g. maleimide) specific for thiol groups of the protein moiety of the oligonucleotide-protein conjugate and **b)** reacting the thiol group of the protein with the thiol-reactive second reactive group of the heterobifunctionally derivatized oligonucleotide to form a oligonucleotide/protein conjugate. See Reddy et al: col. 5, lines 51-63; heterobifunctional linkers of col. 6, line 8 – col. 7, line 13; reaction scheme of col. 19; Example 1. This method is the same method described in instant claim 1 with the sole exception being that the reactive thiol group of the protein used in Reddy et al is a native thiol group while the thiol group of the protein used in the instant invention is an added thiol group. Reddy et al is further applied for its description of parameters which are routinely modified in the art as set forth in paragraph **5)**, second subparagraph, of the February 18, 2004 Office action.

Garman et al establish that it is well known in the art that thiol containing proteins which have either native or introduced thiol groups can be coupled to oligonucleotides using conventional

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heterobifunctional linkers of the type described by Reddy et al (e.g. SMCC). See Garman et al: the thiol groups of col. 5, lines 36-42; the heterobifunctional linkers of columns 2-4.

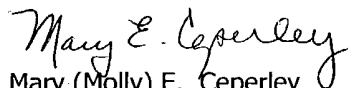
Given the description of Garman et al that both native and introduced protein thiol groups can be used as functional moieties for the conjugation of proteins to oligonucleotides via heterobifunctional reagents, it would be obvious to substitute an introduced protein thiol group (as described by Garman et al) as an equivalent for the native protein thiol group in the method of Reddy et al with the expectation of obtaining a similarly useful protein-oligonucleotide conjugation method and the corresponding product produced by the method, as claimed. Claim 22 of Reddy et al describes a ligand binding assay which corresponds to the assay of instant claim 63.

4) Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary (Molly) E. Ceperley whose telephone number is (571) 272-0813. The examiner can normally be reached from 8 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le, can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 08, 2004

  
Mary (Molly) E. Ceperley  
Primary Examiner  
Art Unit 1641